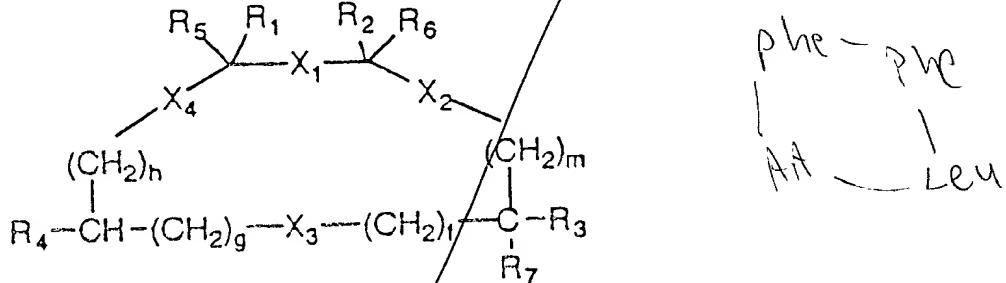


IN THE CLAIMS:

Kindly amend Claims 1-3, 5-13 and add Claim 15 under the provisions of 37 CFR §1.121(a) as follows:

A1
Ab5

1. (Amended) A monocyclic compound having the general formula (I):



in which:

X₁, X₂, X₃, X₄, which may be the same or different from one another, is selected from the group consisting of -CONR-, -NRCO-, -OCO-, -COO-, -CH₂NR-, -NR-CH₂- and CH₂-CH₂ where R is H or a C₁₋₃ alkyl or benzyl;

f, g, h, m, which may be the same or different from one another, represent a number selected from the group consisting of 0, 1 and 2;

R₁ and R₂, which may be the same or different from one another, represent a -(CH₂)_r-Ar group, where r= 0, 1, 2 and where Ar is an aromatic group selected from the group consisting of: benzene, naphthalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, and benzo-imidazole, said Ar group being possibly substituted with a maximum of two residues selected from the group consisting of C₁₋₃ alkyl or halo-alkyl, C₁₋₃ alkoxy, C₂₋₄ amino-alkoxy, halogen, OH, NH₂ and NR₁₃R₁₄ where R₁₃ and R₁₄, which may be the same or different from one another, represent hydrogen or C₁₋₃ alkyl;

R³ ↛ wherein R₃ is selected from the group consisting of:

-hydrogen,

-linear or branched alkyl having the formula C_nH_{2n+1}, with n= 1-5, cyclo-alkyl or alkylcyclo-alkyl groups having the formula C_nH_{2n-1}, with n= 5-9,

-(CH₂)_r-Ar₁, where r= 0, 1, 2 and where Ar₁ is an aromatic group selected from the group consisting of: benzene, naphthalene, thiophene, benzothiophene, pyridine,

A/
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quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, and benzo-imidazole, said Ar₁ group being possibly substituted with a maximum of two residues selected from the group consisting of C₁₋₃ alkyl or halo-alkyl, C₁₋₃ alkoxy or amino-alkoxy, halogen, OH, NH₂ and NR₁₃R₁₄, where R₁₃ and R₁₄, which may be the same or different from one another, represent hydrogen or C₁₋₃ alkyl; wherein R₄ is selected from the group consisting of:

- hydrogen or C₁₋₆ alkyl,
- L-Q, where L is a chemical bond or a linear or branched C₁₋₆ alkyl residue and Q is selected from the group consisting of:
 - i) H, OH, OR₉, NH₂, NR₉R₁₀, guanidine, sulfate, phosphonate and phosphate where R₉ and R₁₀, which may be the same or different from one another, represent a hydrogen C₁₋₃ alkyl group, C₁₋₃ hydroxyalkyl, C₁₋₃ dihydroxyalkyl, C₁₋₃alkyl-CONHR₁₂, C₁₋₃alkyltetrazole, C₁₋₃alkyl-COOH or wherein R₉R₁₀ joined together form with the N-atom a saturated 4-6 membered heterocycle possibly containing a further heteroatom selected from the group consisting of N, O and S and wherein R₁₂ is a mono-, di-, tri-glycosidic group possibly protected with one or more C₁₋₃-acyl groups or substituted with amino-groups or C₁₋₃ acylamino-groups;
 - ii) COOH, tetrazole, SO₂NH₂, SO₂NHCOOR₈, CONHR₈, NHCOR₈, where R₈ represents a linear or cyclic C₁₋₆ alkyl chain containing one or more polar groups selected from the group consisting of: OH, NH₂, NR₁₅R₁₆, COOH, CONHR₁₂, PO₃H, SO₃H and OR₁₁ and where R₁₅ and R₁₆, which may be the same or different from one another, represent a hydrogen or C₁₋₃ alkyl group, and where R₁₁ is a C₁₋₃ alkyl or C₂₋₄ amino-alkyl chain, R₁₂ is a mono-, di-, tri-glycosidic group possibly protected with one or more C₁₋₃acyl groups or substituted with amino-groups or C₁₋₃acylamino-groups or R₁₅R₁₆ joined together form with the N-atom a saturated 4-6 membered heterocycle possibly substituted with C₁₋₃alkyl-groups or with saturated 4-6 membered heterocycle-groups containing at least an N-atom;
 - iii) COOR₁₇, CONHR₁₂, OR₁₂ where R₁₂ is a mono-, di-, tri-glycoside group possibly protected with one or more C₁₋₃ acyl groups or substituted with amine or C₁₋₃ acylamine groups and R₁₇ is a group R₁₂ as above defined or a group

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C_{1-3} alkyl, C_{1-3} alkylphenyl, wherein the phenyl-group can be substituted with a group OH, NO_2 , NH_2 , CN, CH_3 , Cl, Br;

R_5 , R_6 , R_7 , which may be the same or different from one another, represent a hydrogen or C_{1-3} alkyl group; or an acceptable salt or enantiomer thereof.

2. (Amended) Compounds according to Claim 1, in which:

f , g , h , m , which may be the same or different from one another, may be 0 or 1;

R_1 and R_2 which may be the same or different from one another, represent the side chain of a natural amino acid selected from the group consisting of tryptophan, phenylalanine, tyrosine and histidine, or the side chain of a non-natural amino acid selected from the group consisting of:

tryptophan and phenyl alanine, either mono- or di-substituted with residues selected from the group consisting of C_{1-3} alkyl or halo-alkyl, C_{1-3} alkoxy or amino-alkoxy, halogen, OH, NH_2 and $NR_{13}R_{14}$, where R_{13} and R_{14} , which may be the same or different from one another, represent a hydrogen or C_{1-3} alkyl group;

R_3 is selected from the group consisting of:

– linear or branched alkyl having the formula C_nH_{2n+1} with $n = 1-5$ (selected from the group consisting of methyl, ethyl, propyl, isopropyl, n-butyl and t-butyl) cycloalkyl or alkylcycloalkyl of formula C_nH_{2n-1} with $n = 5-9$ (selected from the group consisting of: cyclopentyl, cyclohexyl and methylcyclohexyl)

– $(CH_2)_r-Ar_1$, where $r = 1$ or 2 and where Ar_1 is an aromatic group selected from the group consisting of: α -naphthyl, β -naphthyl, phenyl, indole, said Ar_1 group being possibly substituted with a maximum of two residues selected from the group consisting of: C_{1-3} alkyl, CF_3 , C_{1-3} alkoxy, Cl, F, OH and NH_2 ;

R_4 represents an L-Q group where:

L is a chemical bond or CH_2 , and

Q is selected from the group consisting of:

– OH, NH_2 , NR_9R_{10} and OR_{11} , and where R_9 and R_{10} , which may be the same or different from one another, represent a hydrogen or C_{1-3} alkyl group, C_{1-3} hydroxy alkyl, C_{1-3} dihydroxyalkyl, C_{1-3} alkyl-CONHR₁₂ (wherein R_{12} is a monoglycosidic

group derived from D or L pentoses or hexoses (selected from the group consisting of ribose, arabinose, glucose, galactose, fructose, glucosamine and galactosamine and their N-acetylated derivatives)), $C_{1-3}\text{alkyltetrazole}$, $C_{1-3}\text{alkyl-COOH}$ or wherein R_9R_{10} are joined together to form with the N atom a morpholine or a piperidine ring and where R_{11} is a C_{1-3} alkyl chain, or a C_{2-4} amino-alkyl chain;

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cont.

*All
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– NHCOR_8 wherein R_8 is a cyclohexane containing from 2 to 4 OH groups, a C₁-alkylchain containing a polar group (chosen in the group consisting of NH_2 , COOH , CONHR_{12} , (wherein R_{12} is as hereabove defined) or [1,4']bipiperidine)

– COOH , COOR_{17} or CONHR_{12} , wherein R_{12} is as hereabove defined and R_{17} is as R_{12} or a group 4-nitrobenzyl.

– R_5 , R_6 , R_7 are H[
in which the carbon atom that carries the substituents R_3 and R_7 has configuration R.

Ch Bla

3. A compound according to Claim 2 selected from:

- (a) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂C₆H₅)-CH₂-NH]}
- (b) Cyclo {-Suc-Trp-Phe-[(S)-NH-CH(CH₂C₆H₅)-CH₂-NH]}
- (c) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂C₆H₁₁)-CH₂-NH]}
- (d) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂C₆H₄(4-OCH₃))-CH₂-NH]}
- (e) Cyclo {-Suc-Trp(5F)-Phe-[(R)-NH-CH(CH₂C₆H₅)-CH₂-NH]}
- (f) Cyclo {-Suc-Trp(Me)-Phe-[(R)-NH-CH(CH₂C₆H₅)-CH₂-NH]}
- (g) Cyclo {-Suc-Phe(3,4-Cl)-Phe-[(R)-NH-CH(CH₂C₆H₅)-CH₂-NH]}
- (h) Cyclo {-Suc-Trp-Phe(3,4-Cl)-[(R)-NH-CH(CH₂C₆H₅)-CH₂-NH]}
- (i) Cyclo {-Suc-Trp-Tyr-[(R)-NH-CH(CH₂C₆H₅)-CH₂-NH]}
- (j) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂C₆H₃-3,4-diCl)-CH₂-NH]}
- (k) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂C₆H₄-4-OH)-CH₂-NH]}
- (l) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂-CH₂-C₆H₅)-CH₂-NH]}
- (m) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂-2-naphthyl)-CH₂-NH]}
- (n) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂-indol-3-yl)-CH₂-NH]}
- (o) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂-5-F-indol-3-yl)-CH₂-NH]}
- (p) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₄-3-F)-CH₂-NH]}
- (q) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₃-3,4-diF-CH₂-NH)]-}
- (r) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₄-4-CF₃-CH₂-NH)]-}
- (s) Cyclo {-Suc-Trp-Phe-[(R)-NH-CH₂-CH(CH₂C₆H₅)-NH]}
- (t) Cyclo {-Suc-Trp-Phe-[(S)-NH-CH₂-CH(CH₂C₆H₅)-NH]}
- (u) Cyclo {-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-(CH₂)₃CO-}

*all
cont.*

- (v) Cyclo {-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-N(CH₃)]-(CH₂)₃CO-}
- (w) Cyclo {-Suc[1(S)-NH₂]-Trp-Phe-[(R)NH-CH(CH₂-C₆H₅)-CH₂NH]-}
- (x) Cyclo {-Suc[1(R)-NH₂]-Trp-Phe-[(R)NH-CH(CH₂-C₆H₅)-CH₂NH]-}
- (y) Cyclo {-Suc[2(S)-NH₂]-Trp-Phe-[(R)NH-CH(CH₂-C₆H₅)-CH₂NH]-}
- (z) Cyclo {-Suc[2(R)-NH₂]-Trp-Phe-[(R)NH-CH(CH₂-C₆H₅)-CH₂NH]-}
- (aa) Cyclo {-Suc[1(S)-NH(CH₃)]-Trp-Phe-[(R)NH-CH(CH₂-C₆H₅)-CH₂NH]-}
- (ab) Cyclo {-Suc[1-COO(CH₂-C₆H₄-4-NO₂)]-Trp-Phe-[(R)NH-CH(CH₂-C₆H₅)-CH₂NH]-}
- (ac) Cyclo {-Suc(1-COOH)-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]}
- (ad) Cyclo {-Suc(1-OH)-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]}
- (ae) Cyclo {-Suc(2-COOH)-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]}
- (af) Cyclo {-Suc(2-OH)-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]}
- (ag) Cyclo {-Suc[1(S)-(2H-tetrazolyl-5-ylmethyl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-}. TFA
- (ah) Cyclo {-Suc[1(S)-(morpholin-4-yl)]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-}. TFA
- (ai) Cyclo {-Suc[1(S)-N(CH₃)₂]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-}. TFA
- (aj) Cyclo {-Suc[1(S)-(piperidin-4-yl)]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-}. TFA
- (ak) Cyclo {-Suc[1(S)-(N(CH₂CH₂OH)₂)]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-}. TFA
- (al) Cyclo {-Suc[1(S)-(N(CH₂CH(OH)CH₂OH)]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-}. TFA
- (am) Cyclo {-Suc[1(S)-(3-carboxypropanoyl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-}.
- (an) Cyclo {-Suc[1(S)-[3-N'-β-D-glucopiranos-1-yl)-carboxamidopropanoyl]amino]-Trp-Phe-[(R)NH-CH(CH₂-C₆H₅)-CH₂NH]-}
- (ao) Cyclo {-Suc[1(S)-[(carboxymethyl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-}. TFA
- (ap) Cyclo {-Suc[1(S)-[N'-β-D-glucopiranos-1-yl)-carboxyamidomethyl]amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-} TFA

AI

Conclude

(aq) Cyclo {-Suc[1(S)-(chanyl)amine]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-} TFA

(ar) Cyclo {-Suc[1(S)-(4-aminobutanoyl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-} TFA

(as) Cyclo {-Suc[1(S)-[1,4')bipiperidin-1-yl]acetamido]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-} TFA

(at) Cyclo {-Suc[1-N-(β -D-glucopiranos-1-yl)-carboxyamido]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-} TFA

(au) Cyclo {-Suc[1(S)-[N'-(2-N-acetyl- β -D-glucopiranos-1-yl)-carboxyamido]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂-NH]-}.

Q2

GBA

5. (Amended) A composition comprising a compound of general formula (I) according to Claim 1 in combination with a suitable carrier or excipients.

6. (Amended) A composition according to Claim 5, adapted for use as tachykinin antagonists.

7. (Amended) A composition according to Claim 6, adapted for use as antagonists of the human NK-2 receptor.

8. (Amended) A composition according to Claim 7, adapted for use in the treatment of the bronchospastic and inflammatory component of asthma, coughing, pulmonary irritation, intestinal spasms, spasms of the biliary tract, local spasms of the bladder and of the ureter during cystitis, and kidney infections and colics.

Sub C1

9. (Amended) A composition according to Claim 7, adapted for use as anxiolytics.

10. (Amended) A method of antagonizing tachykinin in a mammal in need thereof comprising contacting tachykinin peptide receptors with a compound according to Claim 1 for a time and under conditions effective to antagonize said tachykinin receptors.

Q2 (AB)
Concluded

11. (Amended) A method of antagonizing an NK-2 receptor in a mammal in need thereof comprising contacting an NK-2 receptor with a compound according to Claim 1 for a time and under conditions effective to antagonize an NK-2 receptor.

12. (Amended) A method of antagonizing an NK-2 receptor in a mammal afflicted with asthma comprising contacting an NK-2 receptor with a compound according to Claim 1 for a time and under conditions effective to antagonize an NK-2 .

13. (Amended) A method of antagonizing an NK-2 receptor in a mammal afflicted with an anxiety disorder comprising contacting an NK-2 receptor with a compound according to Claim 1 for a time and under conditions effective to antagonize an NK-2 receptor.

Q3

15. (New) A mixture comprising two or more compounds according to Claim 1.